Doc Code: AP.PRE.REQ

PTO/SB/33 (12-08)
Approved for use through 07/31/2012. OMB 0651-00xx
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PRE-APPEAL BRIEF REQUEST FOR REVIEW	Docket Number (Optional) 03-235

Certificate of Electronic Transmission
Under 37 C.F.R. §1.8

I hereby certify that this correspondence and any document referenced herein are being electronically filed with the USPTO via EFS-Web on July 23, 2010.

Nancy Joyce Simmons
(Printed Name of Person Sending Correspondence)

/nancy joyce simmons/
(Signature)

Application Number	Filed
10/777,802	February 12, 2004

First Named Inventor: Sheng-Ping Zhong

Art Unit	Examiner
1615	Hasan Syed Ahmed

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- [ ] applicant /inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- [x] attorney or agent of record. Registration number 34,297
- [ ] attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34.

/David B. Bonham/
Signature

David B. Bonham
Typed or printed name

703-433-0510
Telephone number

July 23, 2010
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

[x] *Total of 1 forms are submitted.

i

Rejection Under 35 U.S.C. §103(a) Based on Weber

The Examiner has rejected Claims 1, 17, 19, 21-23, 25, 27 and 28 under 35 U.S.C. §103(a) over Weber, WO2003/026532 ("Weber"). It is respectfully submitted that this rejection is in error.

For a proper obviousness rejection under 35 U.S.C. 103, the differences between the subject matter sought to be patented and the prior art must be such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains. 35 U.S.C. §103. The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. MPEP 2141. " '[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.' " *KSR International Co.* v. *Teleflex Inc.*, 550 U.S. ___, 82 USPQ2d 1385 (2007), quoting *In re Kahn ,* 441 F.3d 977, 988, (Fed. Cir. 2006). It should be noted that the prior art reference (or references when combined) must teach or suggest all the claimed features. "When determining whether a claim is obvious, an examiner must make 'a searching comparison of the claimed invention – *including all its limitations* – with the teaching of the prior art.' … Thus, 'obviousness requires a suggestion of all limitations in a claim.' …" *Ex parte Wada and Murphy*, BPAI Appeal No. 2007-3733, January 14, 2008 (emphasis in original) (citations omitted). In addition, there must be a reasonable expectation of success. See MPEP 2143.02.

Claim 1, the only independent claim presently pending, is directed to an implantable or insertable medical device comprising a release region, said release region comprising:

(a) a polymeric carrier comprising a ***hydrophobic first polymer*** and

(b) drug loaded nanoparticles dispersed within said polymeric carrier, said drug loaded nanoparticles comprising: ***silicate particles*** comprising a layered silicate material; ***a hydrophilic first therapeutic agent***; and a ***hydrophilic second polymer***,

wherein the first therapeutic agent and hydrophilic second polymer are structurally associated with the silicate particles in that the first therapeutic agent and hydrophilic second polymer occupy spaces between adjacent layers of the silicate material of each silicate particle to form a depot for the first therapeutic agent.

The Examiner argues the following at page 6 of the final Office Action mailed April 1, 2010 (emphasis added):

> Weber does not provide an explicit example or embodiment of an implantable or insertable medical device comprising a release region, in turn comprising a polymeric carrier comprising a first polymer and drug loaded nanoparticles dispersed within said polymeric carrier, said drug loaded nanoparticles comprising a layered silicate material and a first therapeutic agent. However, based on the teachings cited above, ***Weber explicitly teaches each of the structural features being claimed in the same configuration being claimed, i.e. nanoparticles comprising a therapeutic agent dispersed in a polymer which in turn is coated onto an implantable or insertable medical devise.*** As such, Weber reads on the instant application, as claimed.

Applicant respectfully disagrees. First, the Examiner fails to note that the claimed invention comprises a first polymer and a second polymer, specifically ***a hydrophobic first polymer and a hydrophilic second polymer***.

Moreover, it is noted that the present invention claims that "the first therapeutic agent and hydrophilic second polymer are structurally associated with the silicate particles in that ***the first therapeutic agent and hydrophilic second polymer occupy spaces between adjacent layers of the silicate material of each silicate particle to form a depot for the first therapeutic agent***". (emphasis added).

In an attempt to address this issue, the Examiner further argues the following at page 7 of the final Office Action (emphasis added):

> Weber does not explicitly disclose the placement of the therapeutic agent in the spaces between adjacent layers of the silicate material of each silicate particle to form a depot. However, Weber teaches nanoparticles made of the same material being instantly claimed, i.e., smectite silicate (see page 9, line 4), and a hydrophilic therapeutic agent (see page 11, line 17 - page 12, line 6; e.g. acetylsalicylic acid) associated with said nanoparticles (see, e.g., page 11, lines 14-15). ***The placement of a hydrophilic therapeutic agent in the spaces between the adjacent layers of the silicate material is a property of interaction between the silicate and the therapeutic agent.*** Properties are the same when the structure and composition are the same. In re Fitzgerald, 205 USPQ 594.

Applicant again respectfully disagrees.

First, Weber does not appear to disclose a combination of a hydrophobic first polymer and a hydrophilic second polymer as claimed. The Examiner attempts to address this issue on page 8 of the final Office Action as follows: "Weber teaches that the matrix material can be a polymer blend (see page 8, line 4). As such, Weber envisions using a combination of any of the matrix materials listed in the subsequent paragraph (see page 8, lines 5-15) which includes a hydrophobic

polymer such as a polyolefin block copolymer and a hydrophilic polymer such as a polyacrylic polymer."

In this regard, "polyacrylics" as disclosed in Weber can be either hydrophilic (e.g., sodium polyacrylate) or hydrophobic (e.g., an alkyl acrylate such as butyl acrylate, among others).

Moreover, while Weber teaches at page 8, line 4 that "the matrix material may be a metal alloy, copolymer or polymer blend," this falls far short of describing a matrix material comprising a hydrophobic first polymer and a hydrophilic second polymer as claimed.

For example, as noted above, while describing classes of polymers that include hydrophilic polymers, Weber does not appear to actually describe a hydrophilic polymer as claimed.

Moreover, the claims require a specific *combination* of a *hydrophobic* first polymer and a *hydrophilic* second polymer, a combination that one of ordinary skill in the art (indeed, a high school chemistry student) would recognize as involving two polymers that are *incompatible* with one another, much as vinegar and oil are incompatible. If anything, one of ordinary skill in the art would be avoided such a combination.

As stated in MPEP 2142: "The tendency to resort to "hindsight" based upon applicant's disclosure is often difficult to avoid due to the very nature of the examination process. However, impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art." Here, the prior art does not support a conclusion of obviousness absent the hindsight gained from Applicant's disclosure.

It is further noted that, in the presently claimed invention, the hydrophilic polymer is not employed as a blending polymer for use with the hydrophobic polymer as proposed by the Examiner but rather: "the first therapeutic agent and hydrophilic second polymer occupy spaces between adjacent layers of the silicate material of each silicate particle to form a depot for the first therapeutic agent."

Finally, although not explicitly stated, the Examiner's argument that "placement of a hydrophilic therapeutic agent in the spaces between the adjacent layers of the silicate material is a property of interaction between the silicate and the therapeutic agent" constitutes an allegation of inherency on the Examiner's part.

In this regard, a holding of inherency must flow as a necessary conclusion from the prior art, not simply a possible one. The fact that a certain result or characteristic ***may*** occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In*

re Rijckaert, 9 F.3d 1531, 1534, 28 U.S.P.Q.2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 U.S.P.Q. 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" *In re Robertson*, 169 F.3d 743, 745, 49 U.S.P.Q.2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted); MPEP 2112 IV.

Here, it is by no means "clear that the missing descriptive matter is necessarily present in the thing described in the reference."

First, as noted above, "polyacrylics" as disclosed in Weber are not *necessarily* hydrophilic (they can be hydrophobic).

Second, even assuming for the sake of argument that a hydrophilic polymer were to be disclosed, the "blend" as disclosed in Weber is not *necessarily* a blend of hydrophobic and hydrophilic polymers as claimed. For example, the blend can be a blend of two hydrophobic polymers. (Moreover, as noted above, the specific combination of a hydrophobic first polymer and a hydrophilic second polymer in a blend would constitute an *incompatible pairing,* which one of ordinary skill in the art would have been motivated to avoid.)

Finally, even assuming for the sake of argument that one of ordinary skill in the art were to somehow wind up selecting a combination of (a) a *hydrophobic* first polymer, (b) a *hydrophilic* second polymer, (c) a *hydrophilic* first therapeutic agent and (d) a *layered silicate material* (from the many nanoparticle materials described in Weber), there is still no reason to be believe that one would necessarily create a release region "wherein the first therapeutic agent and hydrophilic second polymer are structurally associated with the silicate particles in that the first therapeutic agent and hydrophilic second polymer occupy spaces between adjacent layers of the silicate material of each silicate particle to form a depot for the first therapeutic agent," *without following a procedure that would result in such an association* (e.g., without first loading the silicate particle with the hydrophilic first therapeutic agent and hydrophilic second polymer, followed by introduction to the hydrophobic first polymer, as described in the specification, see, for instance, the Example).

For at least the above reasons, it is respectfully submitted that the Examiner's rejection is in error.

Rejection Under 35 U.S.C. § 103(a) Based on Weber in View of Weber II

The Examiner has rejected Claims 1 and 3 under 35 U.S.C. §103(a) based on Weber in view of Weber et al. U.S. Patent No. 6,743,463 ("Weber II").

Claims 1 and 3 are patentable over Weber II for at least the reasons set forth in the preceding section. Weber II, which is cited for its disclosure of halofuginone as a therapeutic agent, does not make up for the above-noted deficiencies in Weber.

For at least the preceding reasons, withdrawal of the outstanding rejection under 35 USC 103(a) is respectfully requested.